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Playing the numbers game

Are you really getting more?

The number of disorders screened for by different testing labs is a hot topic in the world of newborn screening.

When Hawai'i began screening newborns for over 30 inherited disorders in September 2003, we thought we were on the cutting edge of technology. However, with commercial laboratory Pediatrix declaring it can screen newborns for over 50 disorders and California predicting it can screen newborns for as many as 80 disorders, many parents have been left scratching their heads over the screening number discrepancies.

To help clear the confusion, we have put together a table comparing the disorders screened for, or projected to be screened for, by four different laboratories. We have also included a list of newborn screening disorders recommended by the American College of Medical Genetics (ACMG). The table is located in the middle section.

In creating the table, we found that each laboratory uses a slightly different method of counting their disorders. To show these different counting methods, we used a system of numbers and bullets. All disorders following a number are individually counted by the testing laboratory. All disorders following a bullet (•) are screened for by the laboratory but are not counted as a separate disorder.

For example, PKU (which is #6 on Hawai'i's list) is divided into four variants: Classical PKU, Hyperphenylalaninemia, Benign PKU, and the Biopterin disorders. In its projected list, California has counted each of the PKU variants as individual disorders, giving rise to four separate disorders on their list. Hawai'i and Baylor, on the other hand, count all the PKU variants as one disorder. This difference in counting disorders and variants largely explains why the total number of disorders screened for by the laboratories in our table (and across the country) are so varied.

So, if a lab announces that they can screen newborns for 30, 50, or even 100 disorders, make sure to find out how they tallied up the disorders on their screening list because they could be playing "The Numbers Game".

Coordinator's Corner

This is a special issue of GeneNews devoted entirely to expanded Newborn Screening. There has been a lot of media coverage of the recommendations for a minimum newborn screening panel supported by the American College of Medical Genetics, March of Dimes, and Department of Health and Human Services. Many people are confused about the number and type of disorders a state or commercial laboratory is reportedly including in their screening panel. We hope that the information in this issue of GeneNews will help clarify some of the confusion surrounding the "numbers game" and help you understand how Hawai'i makes community-based decisions about our newborn screening panel.

If you have further questions or comments, please contact me. You may also contact the Newborn Metabolic Screening Program directly at 733-9069.

Sylvia Au, MS, CGC
sylvia@hawaiigenetics.org
(808) 733-9063

Hawai'i Genetics Program

Hawai`i Department of Health
Children with Special Health Needs Branch

741 Sunset Avenue
Honolulu, HI 96816
(808) 733-9055
(808) 733-9068(fax)

Expanded Newborn Screening Comparative Table

Numbers = disorders are screened for and counted by testing lab.

Bullet (•) = disorders are screened for but not counted as a separate disorder by testing lab.

** Newborn hearing screening is also recommended, but is not included in our metabolic table.*

Hawaii	California[1]	ACMG*	Baylor	Pediatrix[2]
AAD:	**AAD:**	**AAD:**	**AAD:**	**AAD:**
1) ARG	1) 5-oxoprolinuria		1) 5-oxoprolinuria	1) 5-oxoprolinuria
2) ASAL	2) ARG	1) ASAL	2) ARG	2) ARG
	3) ASAL		3) ASAL	ASAL
	• Acute onset		• Acute onset	3) Acute onset
	• Chronic onset		• Chronic onset	4) Chronic onset
3) ASAS	4) ASAS	2) ASAS	4) ASAS	ASAS
• Acute onset	• Acute onset		• Acute onset	5) Acute onset
• Chronic onset	• Chronic onset		• Chronic onset	6) Chronic onset
• CIT-type 2	5) CIT-type 2			
				7) CPS[3]
4) HCY	6) HCY	3) HCY	5) HCY	8) HCY
• MAT	7) MAT	4) MAT	6) MAT	9) MAT
	8) HHH	5) HHH	7) HHH	10) HHH[3]
				11) HOGA[3]
5) MSUD	9) MSUD	6) MSUD	8) MSUD	MSUD
• Classical	• Classical		• Classical	12) Classical
• Intermediate	• Intermediate		• Intermediate	13) Intermediate
	10) NKH		9) NKH	
6) PKU	PKU	7) PKU	10) PKU	PKU
• Classical	11) Classical		• Classical	14) Classical
• HPHE	12) HPHE		• HPHE	15) HPHE
• Benign	13) Benign		• Benign	• Benign
• BPT (4 types)[4]	14) BPT (4 types)[4]		• BPT (4 types)[4]	16) BPT (4 types)[4]
7) TYR	TYR		TYR	TYR
• TYR-type 1	15) TYR-type 1	8) TYR-type 1	11) TYR-type 1	17) TYR-type 1
• TYR-type 2	16) TYR-type 2		12) TYR-type 2	18) TYR-type 2
• TYR-type 3	17) TYR-type 3			19) TYR-type 3
• TNTYR	18) TNTYR			20) TNTYR
OAD:	**OAD:**	**OAD:**	**OAD:**	**OAD:**
8) 2MBC	19) 2MBC		13) 2MBC	21) 2MBC
9) 3MCC	20) 3MCC	9) 3MCC	14) 3MCC	22) 3MCC
10) 3MGH	3MGH			23) 3MGH
• 3MGH-type 1	21) 3MGH-type 1			
	22) 3MGH-type 2			
	23) 3MGH-type 3			
	24) 3MGH-type 4			
11) BKD	25) BKD	10) BKD	15) BKD	24) BKD
12) GA-type 1	26) GA-type 1	11) GA-type 1	16) GA-type 1	25) GA-type 1
13) HMG	27) HMG		17) HMG	26) HMG
14) IBD	28) IBD		18) IBD	27) IBD
15) IVA	29) IVA	12) IVA	19) IVA	IVA
• Acute onset	• Acute onset		• Acute onset	28) Acute onset
• Chronic onset	• Chronic onset		• Chronic onset	29) Chronic onset
16) Malonic aciduria	30) Malonic aciduria		20) Malonic aciduria	30) Malonic aciduria
17) MCD	31) MCD	13) MCD		31) MCD
18) MHBD	32) MHBD			
19) MMA	MMA	14) MMA	21) MMA	MMA
• MMA, mut-	33) MMA, mut-		• (unspecified types)	32) MMA, mut-
• MMA, mut 0	34) MMA, mut 0			33) MMA, mut 0
• MMA, cbl A,B	35) MMA, cbl A,B			34) Some cbl types
• MMA, cbl C,D	36) MMA, cbl C,D			35) Maternal B12 deficiency
• MMA, cbl E				
• MMA, cbl F				
• MMA, cbl G				
20) PA	37) PA	15) PA	22) PA	PA
• Acute onset	• Acute onset		• Acute onset	36) Acute onset
• Late onset	• Late onset		• Late onset	37) Late onset
FAOD:	**FAOD:**	**FAOD:**	**FAOD:**	**FAOD:**
21) Carnitine uptake/transport defects[5]	38) CAT		23) CAT	38) CAT
	39) CPT-type 1	16) CUD		39) CPT-type 1
	40) CPT-type 2		24) CPT-type 2	40) CPT-type 2
	41) CUD			41) CUD[3]
				42) DECRD[3]
22) LCHADD	42) LCHADD	17) LCHADD	25) LCHADD	43) LCHADD
• TFP	43) TFP	18) TFP	26) TFP	44) TFP
23) MADD	44) MADD		27) MADD	45) MADD
24) MCADD	45) MCADD	19) MCADD	28) MCADD	46) MCADD
25) SCADD	46) SCADD			47) SCADD
			29) SCHADD	48) SCHADD
26) VLCADD	47) VLCADD	20) VLCADD	30) VLCADD	49) VLCADD
Others:	**Others:**	**Others:**	**Others:**	**Others:**
27) BIO		21) BIO		BIO
				50) Complete
				51) Partial
28) CAH	48) CH	22) CAH		52) CAH
29) CH		23) CH		
	49) EE	24) CF		53) CF
		25) G6PD		
30) GALT	50) GALT	26) GALT		54) GP6PD
	51) Gyrate atrophy			
31) HB				
	52) PRO-type1			
	53) PRO-type 2			
32) SCD	54) SCD	27) SCD		

[1] as of 9/27/04. Expanded screening targeted for 7/2005

[2] based on the StepOne™ supplemental screening program.

[3] according to Pediatrix, the probability of detecting this condition in the immediate newborn period is low.

[4] BPT screening is done on infants with a high phenylalanine level.

[5] is comprised of CAT, CPT-type 1, CPT-type 2, and CUD.

Amino Acid Disorder (AAD):

ARG	Arginase deficiency
ASAL	Argininosuccinate lyase deficiency
ASAS	Argininosuccinate synthetase deficiency (aka: citrullinemia)
BPT	Biopterin cofactor deficiencies
CIT	Citrullinemia
CPS	Carbamoylphosphate synthetase deficiency
HCY	Homocystinuria (aka: cystathionine synthase deficiency)
HHH	Hyperammonemia,hyperornithinemia, homocitrullinuria syndrome
HOGA	Hyperornithinemia with gyral atrophy
HPHE	Hyperphenylalaninemia
MAT	Methionine adenosyltransferase deficiency (aka: hypermethioninemia)
MSUD	Maple syrup urine disease
NKH	Nonketotic hyperglycinemia
PKU	Phenylketonuria
TNTYR	Transient neonatal tyrosinemia
TYR	Tyrosinemia

Organic Acid Disorder (OAD):

2MBC	2-methylbutyryl CoA dehydrogenase deficiency
3MCC	3-methylcrotonyl CoA carboxylase deficiency
3MGH	3-methylglutaconyl CoA hydratase deficiency (aka: 3-methylglutaconic aciduria)
BKD	Beta-ketothiolase deficiency (aka: mitochondrial acetoacetyl-CoA thiolase deficiency)
GA	Glutaric acidemia
HMG	3-hydroxy-3-methylglutaryl CoA lyase deficiency
IBD	Isobutyryl CoA dehydrogenase deficiency
IVA	Isovaleric acidemia
MCD	Multiple carboxylase deficiency
MHBD	2-methyl-3-hydroxybutyryl CoA dehydrogenase deficiency
MMA	Methylmalonic acidemia
PA	Propionic acidemia

Fatty Acid Oxidation Disorder (OAD):

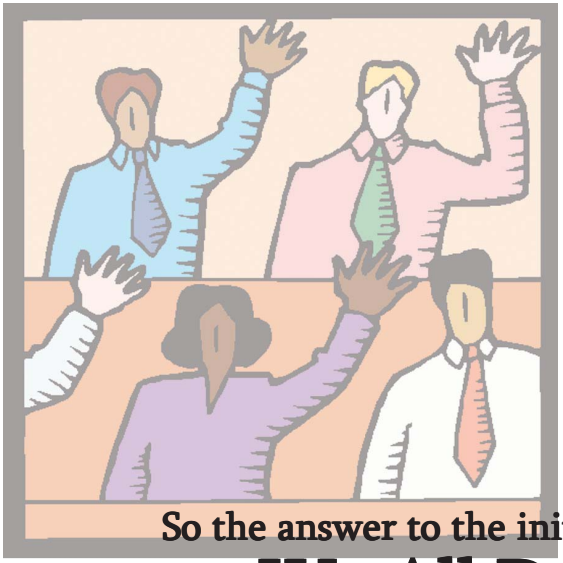
CAT	Carnitine/acylcarnitine translocase deficiency
CPT	Carnitine palmitoyl transferase deficiency
CUD	Carnitine uptake defect (aka: carnitine deficiency; carnitine transporter deficiency)
DECRD	2,4-dienoyl-CoA reductase deficiency
LCHADD	Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency
MADD	Multiple acyl-CoA dehydrogenase deficiency (aka: glutaric acidemia, type 2)
MCADD	Medium chain acyl-CoA dehydrogenase deficiency
SCADD	Short chain acyl-CoA dehydrogenase deficiency
SCHADD	Short chain 3-hydroxyacyl-CoA dehydrogenase deficiency
TFP	Trifunctional protein deficiency
VLCADD	Very long chain acyl-CoA dehydrogenase deficiency

Other:

BIO	Biotinidase deficiency
CAH	Congenital adrenal hyperplasia
CF	Cystic fibrosis
CH	Congenital hypothyroidism
EE	Ethylmalonic encephalopathy
G6PD	Glucose-6-phosphate dehydrogenase deficiency
GALT	Galactosemia
HB	Other hemoglobinopathies
PRO	Prolinemia
SCD	Sickle cell disease

Who Decides?

Since the inception of the Newborn Metabolic Screening Program, decisions about the number and types of metabolic disorders screened for in Hawai'i has been decided by an advisory committee. The Advisory Committee consists of statewide health care providers, parents, hospital administrators, laboratories, health insurance providers, and public health professionals. Currently, the committee has over 30 members. The committee members consider recommendations for adding new disorders by reviewing current published literature, reports from other states, local research data, prevalence of the disorders in Hawai'i, and the cost/benefit associated with early detection and intervention.



Until 1996, the Hawai'i newborn screening panel consisted of only Phenylketonuria and Congenital Hypothyroidism. After much deliberation, the advisory committee approved expanding the panel to seven disorders by adding Biotinidase Deficiency, Congenital Adrenal Hyperplasia, Galactosemia, Hemoglobinopathies, and Maple Syrup Urine Disease. A pilot project to research a new laboratory technology, tandem mass spectrometry, for newborn screening was completed in 2003. Results of the pilot project and data from other states convinced the advisory committee to expand the panel to screen for over 30 disorders. The statewide newborn expanded screening began on September 1, 2003.

The Department of Health and the Advisory Committee will be reviewing the newly published recommendations to determine if any additional testing should be added to our current panel.

So the answer to the initial question is:

We All Decide.

For more information about our genetics activities, please visit: www.hawaiigenetics.org